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CNS Module
Parasitology L2

Parasites Affecting CNS

Free living amoebae

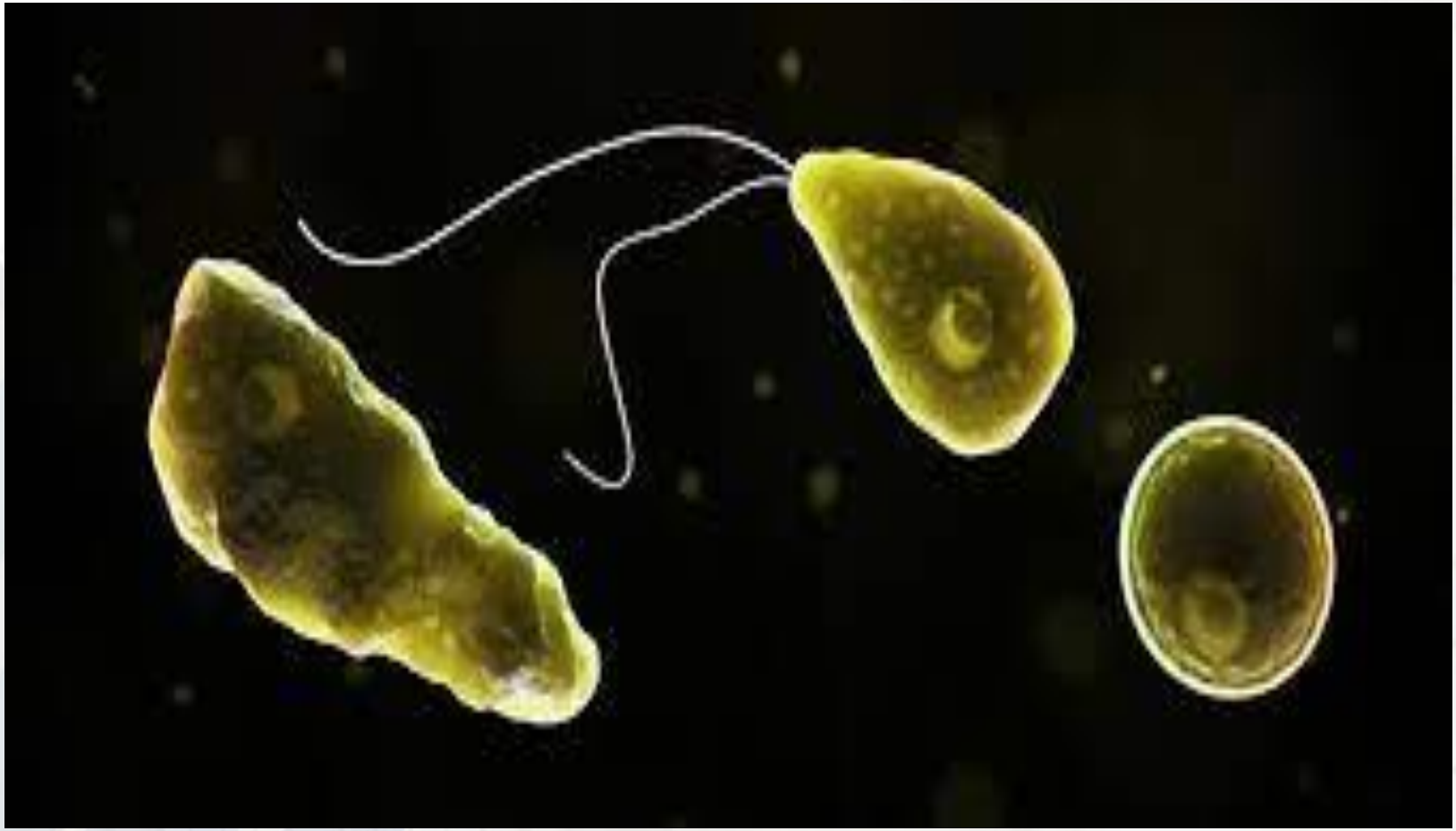
By the end of this lecture the students should:

- List the free-living amoebae.
- Illustrate morphology & life cycle of *Naegleria fowleri* and *Acanthamoeba* spp.
- Discuss clinical picture, diagnosis & treatment of *Naegleria fowleri* and *Acanthamoeba* spp. infections.

PARASITES OF CNS

- **Taenia:**
  1. Cysticercosis (*Taenia solium*).
  2. Coenurosis (*Taenia multiceps*).
- **Free living amoebae:**
  1. *Naegleria fowleri.*
  2. *Acanthamoeba* spp.
- **Trypanosomes:**
  1. African trypansoma.
  2. American trypansoma.

Free living amoebae



Free-living Amoebae

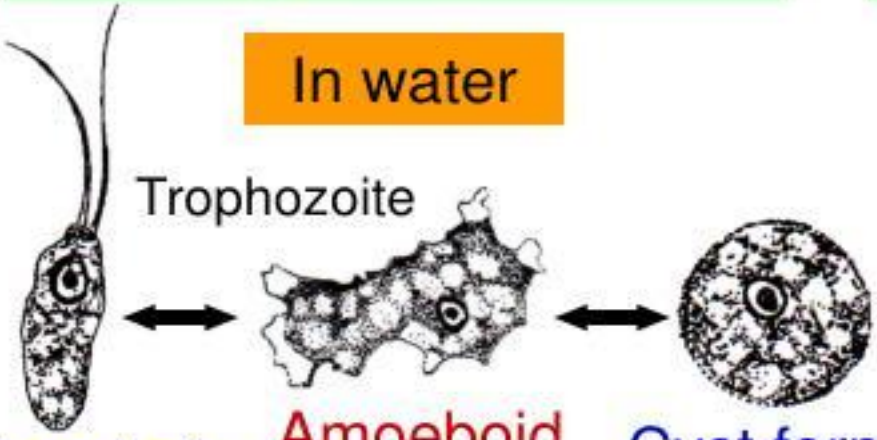
They are amoebae that normally inhabit:

- Water (lakes, swimming pools, air-conditioning units)
- Moist soil.
- Decaying vegetations.

Potentially Pathogenic Free-living amoebae

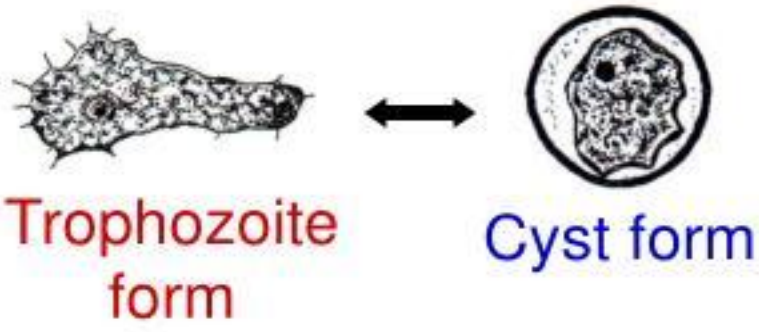
Naegleria fowleri

In water



Acanthamoeba species

In water or air



Free living amoebae

- Are causing three important diseases in man:

1) Acute primary amoebic meningeoencephalitis (PAM) by *N. fowleri*.

2) Chronic granulomatous amoebic encephalitis (GAE) with invasion of other tissues such as lung, nose, skin, etc by *Acanthamoeba.*

3) Chronic amoebic keratitis by *Acanthamoeba* .

1. Naegleria fowleri

Disease:

It causes **acute primary amoebic meningoencephalitis (PAM).**

Geographical distribution:

It is a cosmopolitan parasite lives in fresh warm water in some lakes and ponds, normally feeds on bacteria.

- It is lethal in most cases, with a mortality rate of 98%. Many cases are identified postmortem.

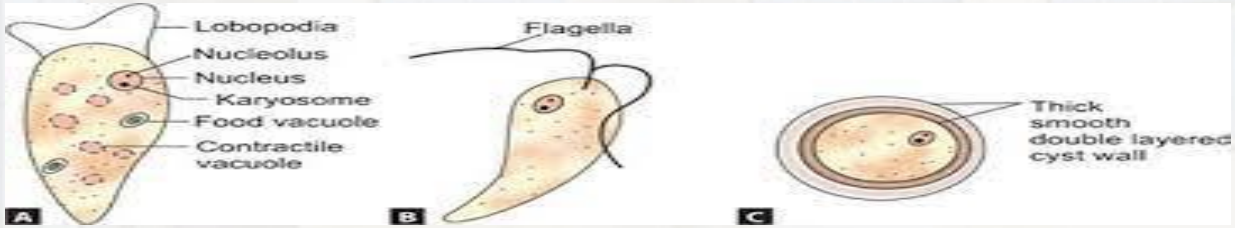
Morphology

The parasite is one of amoebo-flagellates.

1) **Trophozoite:** It has amoeboid shape, 22X7μm in size, and contains nucleus with central karyosome with no peripheral chromatin.

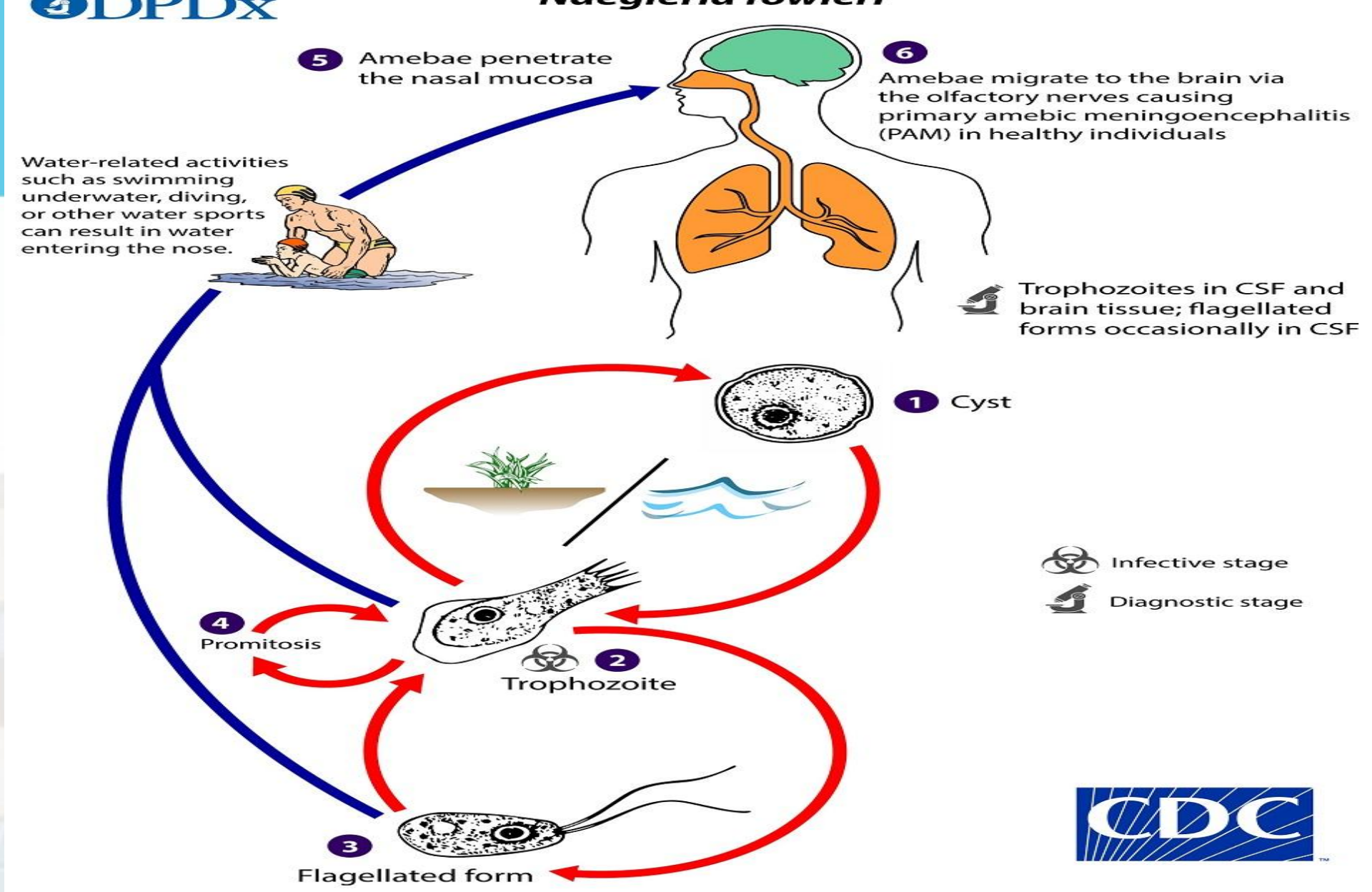
2) **Biflagellate form:** It is 10X7 μm, rapidly motile, pear shaped, with two flagella at the broad end. Motility is typically jerky or spinning movements.

3) **Cyst:** It is a dormant form, round in shape about 9 μm in size and has a thick double wall.



DPDx

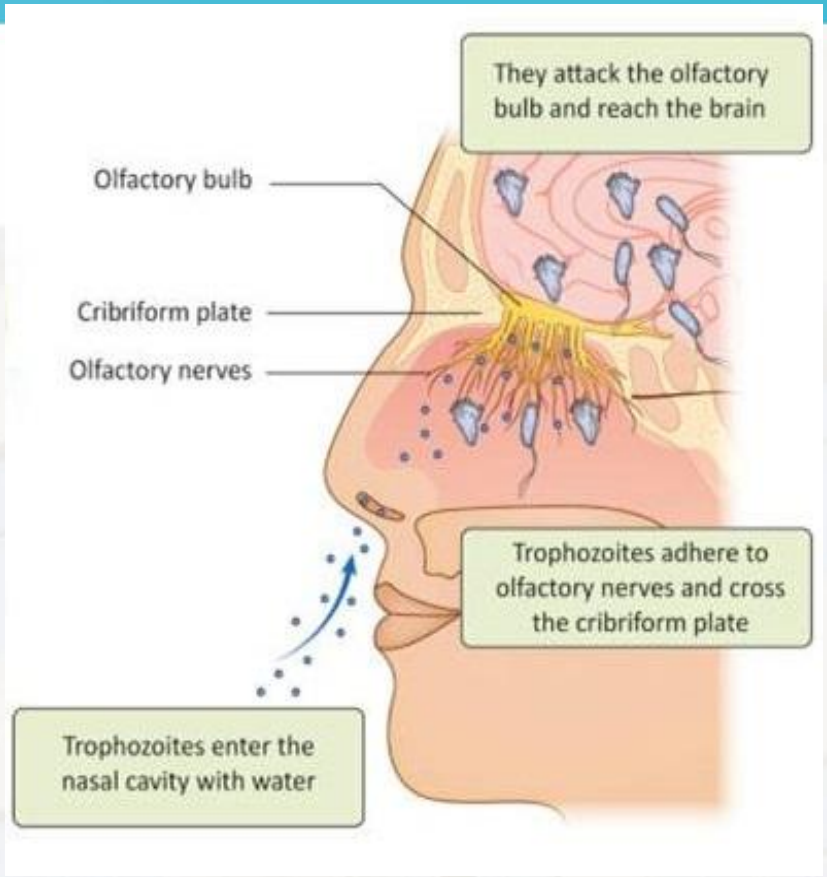
Naegleria fowleri


5 Amebae penetrate the nasal mucosa
6 Amebae migrate to the brain via the olfactory nerves causing primary amebic meningoencephalitis (PAM) in healthy individuals
Water-related activities such as swimming underwater, diving, or other water sports can result in water entering the nose.
Trophozoites in CSF and brain tissue; flagellated forms occasionally in CSF
1 Cyst
Infective stage
Diagnostic stage
4 Promitosis
2 Trophozoite
3 Flagellated form

CDC

Life cycle

- **Habitat: Brain.**
- **Source of infection:** The parasite lives in fresh warm water in some lakes and ponds.
- **Mode of infection**: The amoebae may enter the nasal cavity by inhalation or aspiration of water, dust, or aerosols containing the trophozoites.


They attack the olfactory bulb and reach the brain
Olfactory bulb
Cribriform plate
Olfactory nerves
Trophozoites adhere to olfactory nerves and cross the cribriform plate
Trophozoites enter the nasal cavity with water

- The organisms penetrate the nasal cavity mucosa, through phagocytosis of the olfactory epithelium cells, and migrate via the olfactory nerve to the brain.

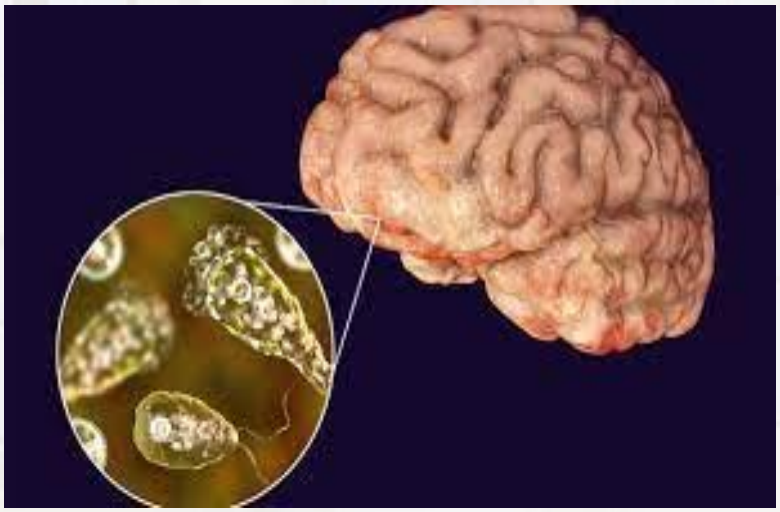
- **The trophozoites form are the only form recognized in humans.**

- They change to the flagellate form when transferred from culture or tissue into water.

- The cysts form is only isolated from nature or agar cultures.

Pathology

- Trophozoite penetrates the brain substance, ingesting the cerebral tissues and induces severe damage, coma and death within a week.



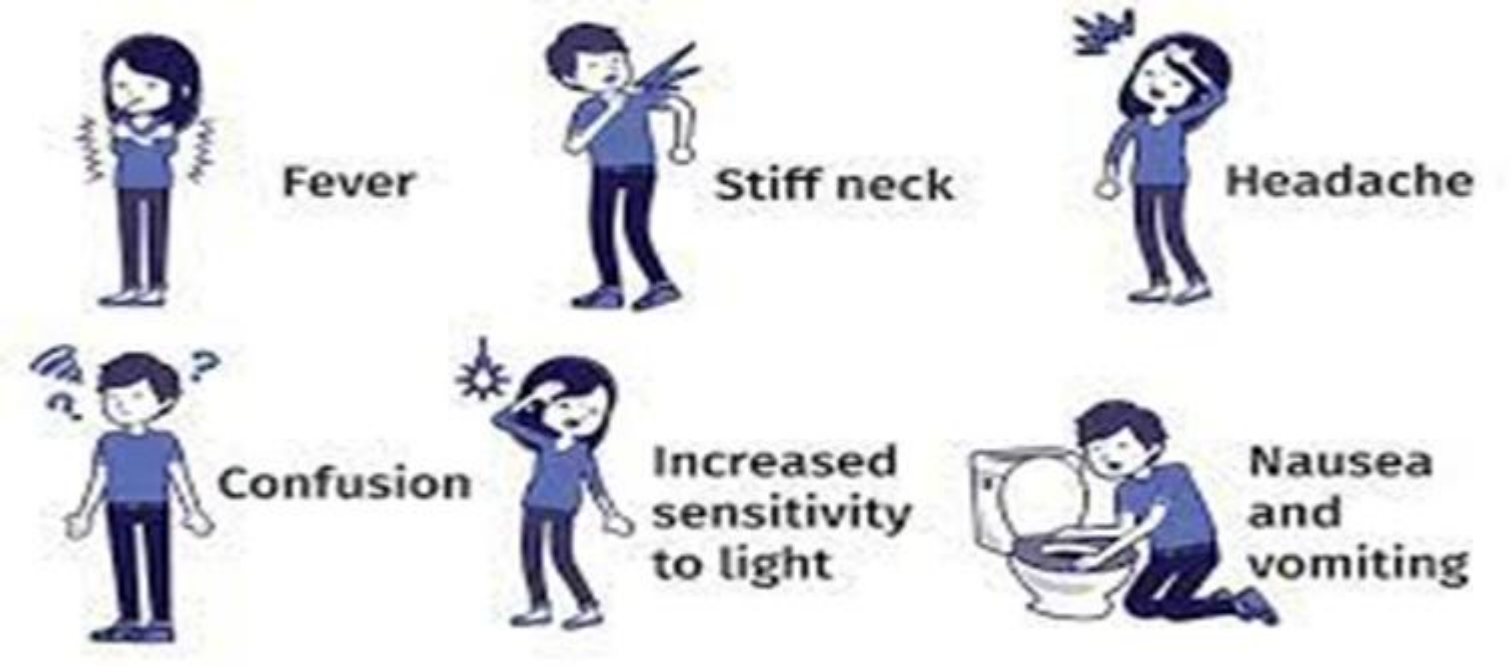
Clinical manifestations

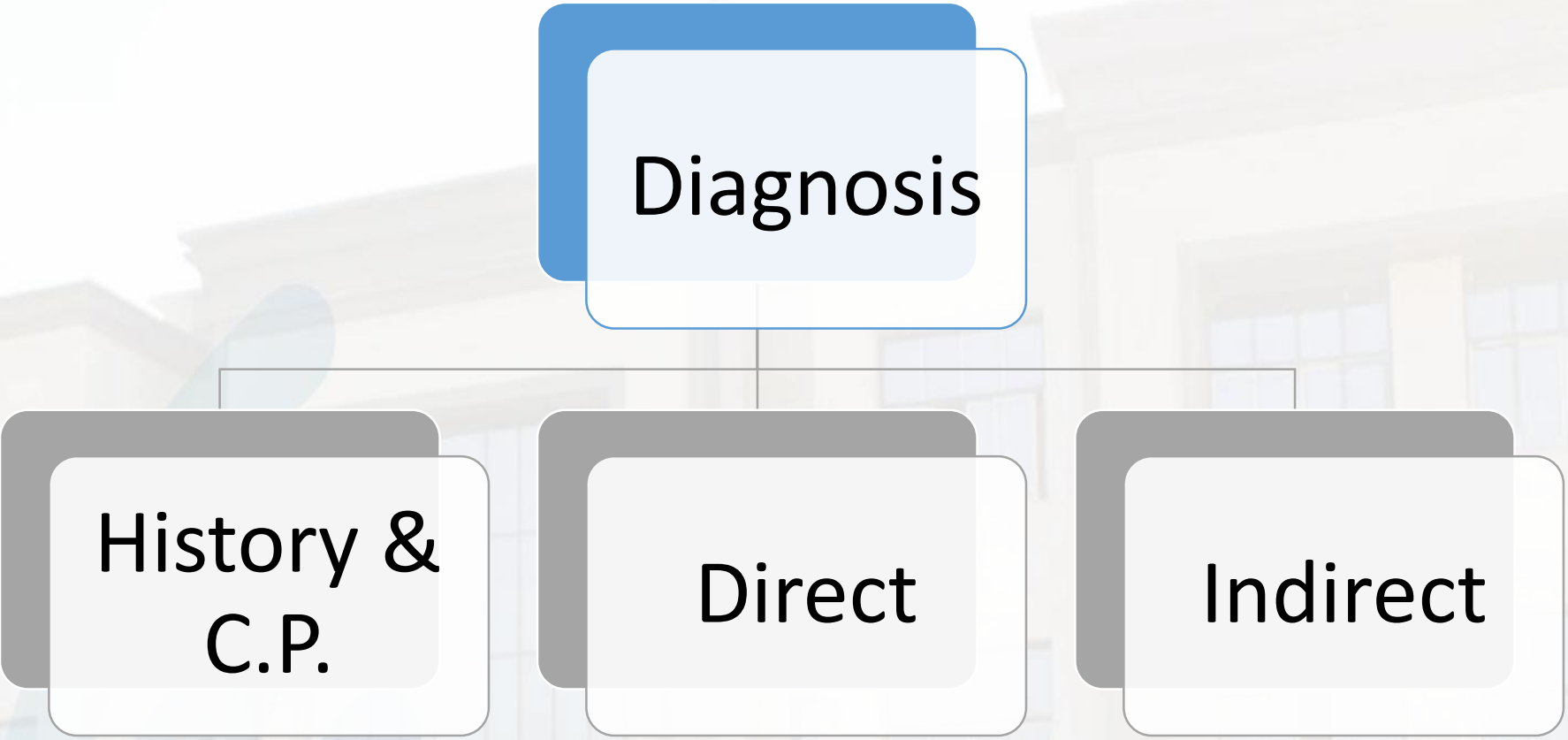
- Clinical manifestations and CSF features are similar to purulent bacterial meningitis but with no response to antibacterial drugs.

- **Onset is acute.**

- The incubation period vary from 2 to as long as 15 days.

- Sore throat and rhinitis may occur.
- Then signs of increased intra-cranial tension develop (headache, vomiting and neck rigidity),
-

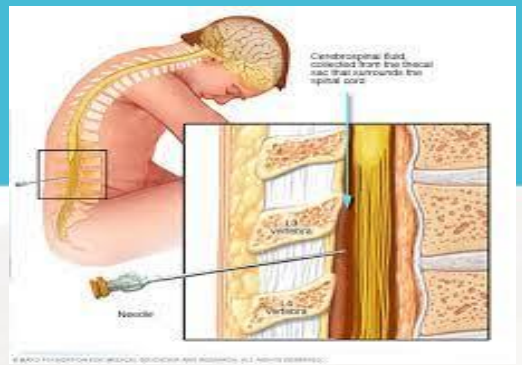



Diagnosis
History & C.P.
Direct
Indirect

Clinical

History of swimming in fresh warm water + clinical manifestations.

Direct



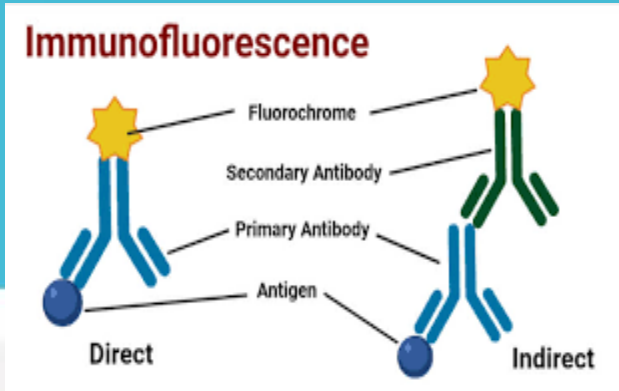
•Specimen: CSF.

•Microscopic examination of the turbid CSF in wet smear is diagnostic by detection of active motile trophozoite with no bacteria. Trophozoites are the only seen stage.

•A drop of CSF added to distilled water allows the transformation of trophozoite into a flagellar form is used as a confirmatory test.

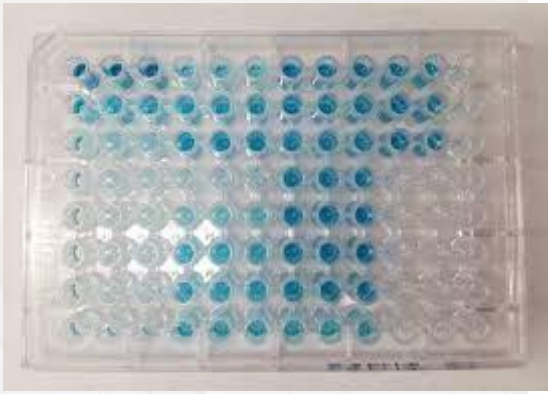
•Microscopic examination of the CSF in stained smear by Giemsa to detect trophozoite.

•Culture on semisolid agar seeded with *E. coli* bacteria is also used.



Indirect

- Serological tests:
- **Antigen detection** by immunofluorescence and EL
- antibody titers in patient sera has no value diagnostic value, because most patients with PAM die before an immune response is mounted.



- PCR

Treatment

- In rare cases, amphotericin B in combination with rifampcin or miconazole has proved to be an effective treatment.

- Miltefosine is the newest drug that has shown ameba-killing activity against free-living amebae, including Naegleria fowleri, in the laboratory.

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Prevention

- Swimming in the stagnant warm fresh water is prohibited.
- Super chlorination of the suspected fresh water is necessary; 2 ppm of chlorine is used 30 min. before use.

2. Acanthamoeba spp.

Disease

Granulomatous amoebic encephalitis (GAE) and/or keratitis and corneal ulceration.

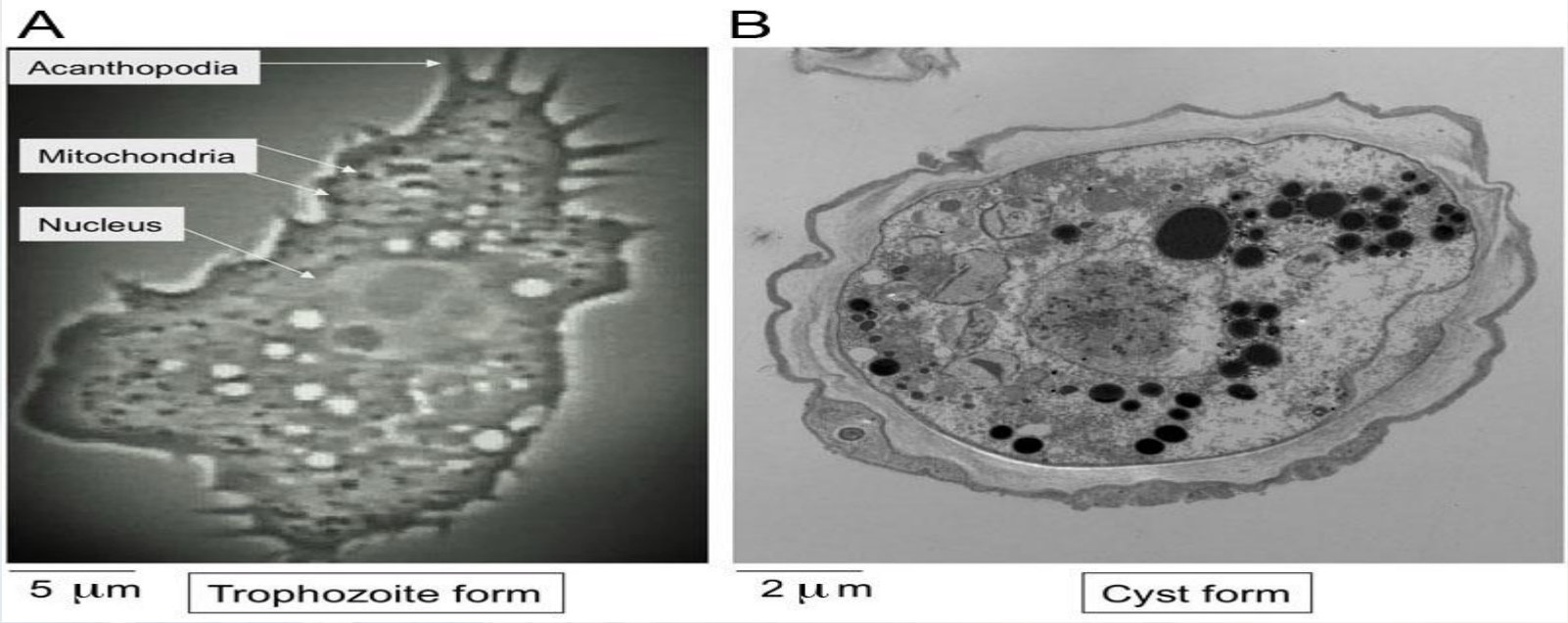
Geographical distribution

Worldwide in moist soil and in fresh and brackish water.

Morphology

1) **Trophozoite:** It has a rough exterior with several projections (acanthopoda) which move slowly. The average diameter being 30 µm. The nucleus is like that of *Naeglaria*.

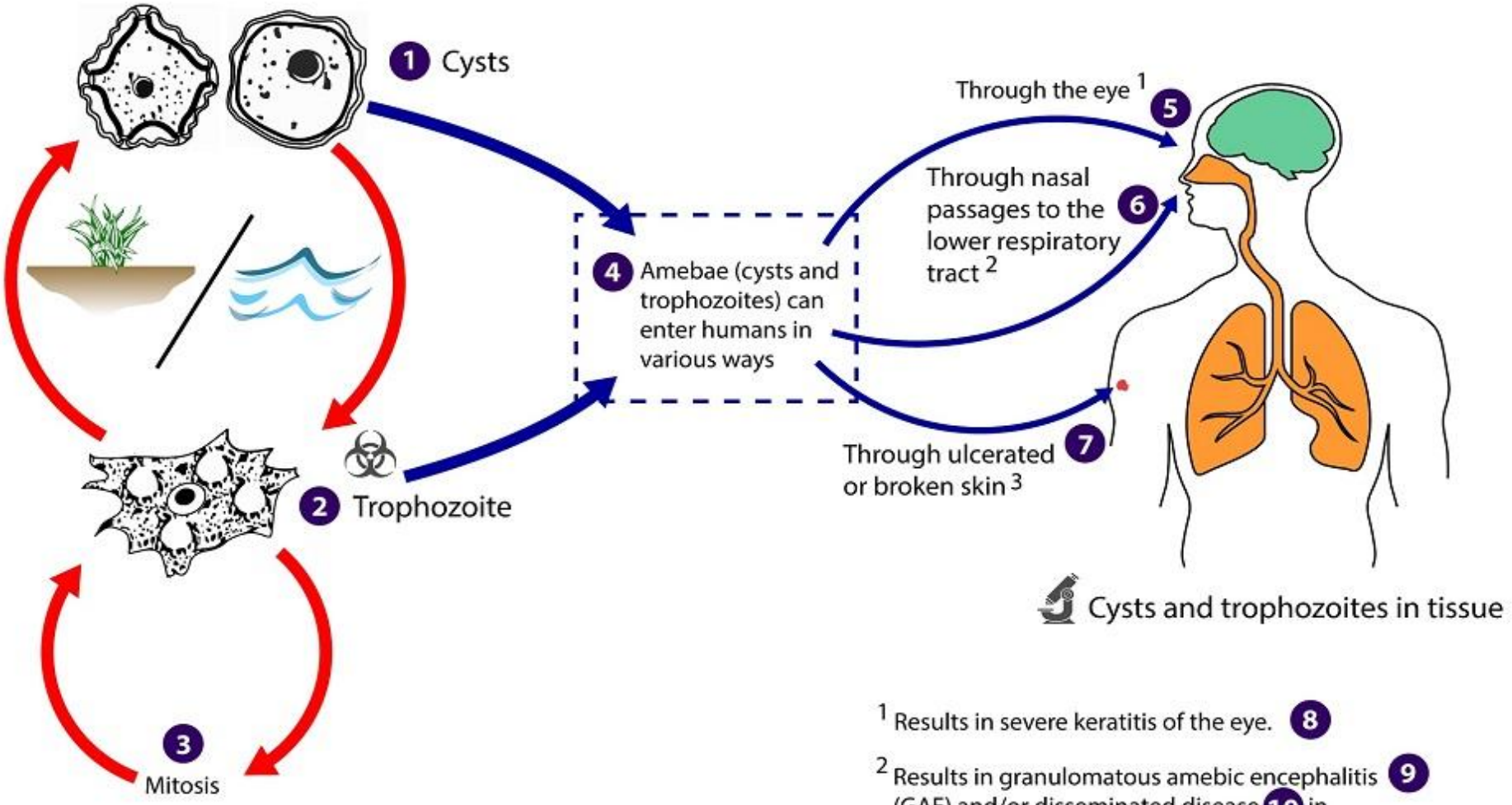
2) **Cyst:** The cyst is round, has a single nucleus with wrinkled outer cyst wall.



DPDx

Acanthamoeba spp.

CDC


1 Cysts
2 Trophozoite
3 Mitosis
4 Amebae (cysts and trophozoites) can enter humans in various ways
Through the eye 1
5
Through nasal passages to the lower respiratory tract 2
6
Through ulcerated or broken skin 3
7
Cysts and trophozoites in tissue

Infective stage

Diagnostic stage

[1] Results in severe keratitis of the eye. 8

[2] Results in granulomatous amebic encephalitis (GAE) and/or disseminated disease 10 in individuals with compromised immune systems. 9

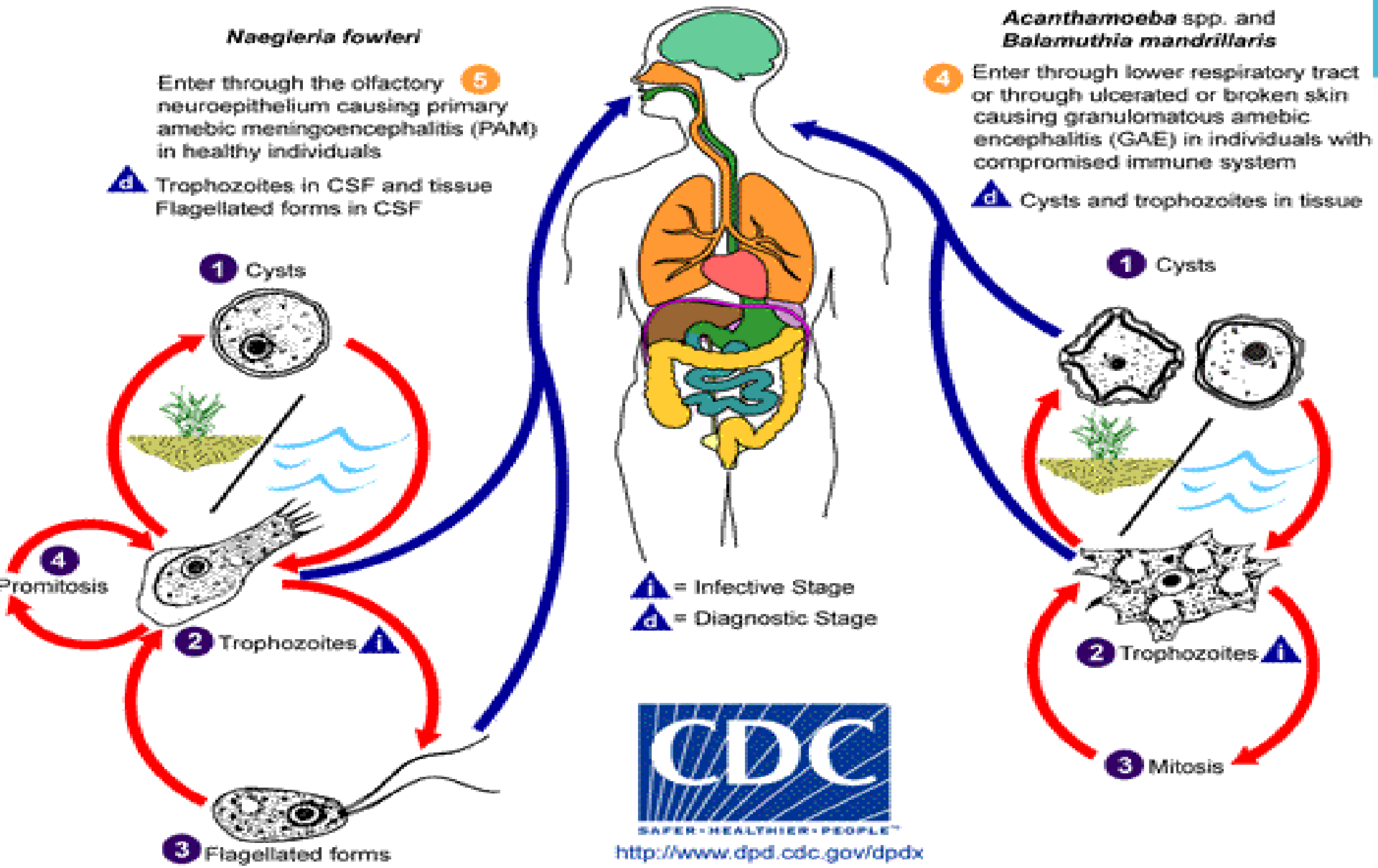
[3] Results granulomatous amebic encephalitis (GAE), disseminated disease 10 or skin lesions 11 in individuals with compromised immune systems. 9

- Man acquires infection by inhalational route by aerosol contaminated with **cyst or trophozoite**, or rarely by direct spread through broken skin or infected eye. .
- The trophozoite and cyst may then reach the target tissue via the blood.

- *Acanthamoeba* infection of the brain is mostly found in immunosuppressed patient.

- Corneal spread with Acanthamoeba occurs following trauma (onset is rapid), contact lens use; especially present in the lens cleaning solution (onset is slow) or contaminated water (onset is slow).

- Both the trophozoite and cyst form could be isolated from human. Dry cysts can survive for several years and can be isolated from dust and air.


Naegleria fowleri
Enter through the olfactory neuroepithelium causing primary amebic meningoencephalitis (PAM) in healthy individuals
5
d Trophozoites in CSF and tissue
Flagellated forms in CSF
1 Cysts
4 Promitosis
2 Trophozoites i
3 Flagellated forms
Acanthamoeba spp. and Balamuthia mandrillaris
4
Enter through lower respiratory tract or through ulcerated or broken skin causing granulomatous amebic encephalitis (GAE) in individuals with compromised immune system
d Cysts and trophozoites in tissue
1 Cysts
2 Trophozoites i
3 Mitosis
i = Infective Stage
d = Diagnostic Stage
CDC
SAFER·HEALTHIER·PEOPLE™
http://www.dpd.cdc.gov/dpdx

Pathology

Brain lesions:

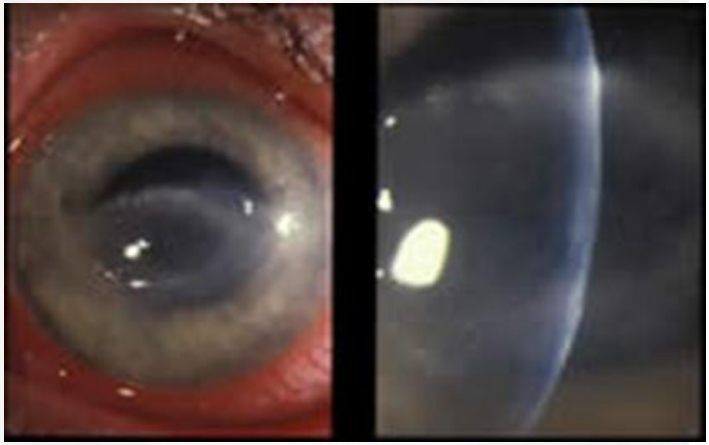
- The brain lesions are essentially focal.

- There are multiple areas of **chronic granulomatous inflammation**.

Clinical manifestations

Ocular Lesions:

- Occur without any brain involvement.
- It is preceded by a history of trauma.
- It begins by a corneal ulcer that progresses and eventually destroys the eye.



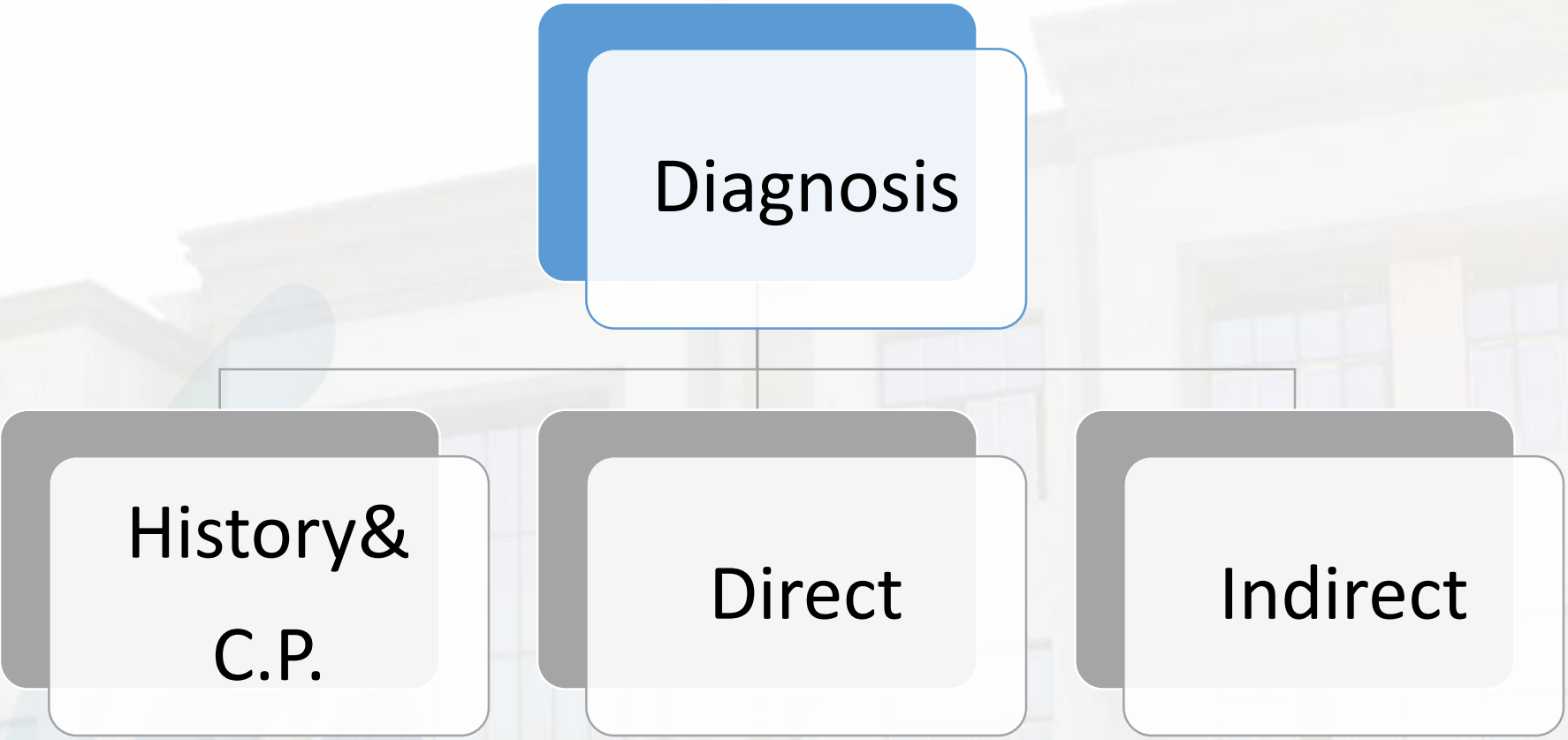
Clinical manifestations

- **Incubation period is from several weeks to months**.

- **Brain lesions:** Headache, fever, local epileptic attacks and midbrain lesions are common.

Cutaneous Lesions:

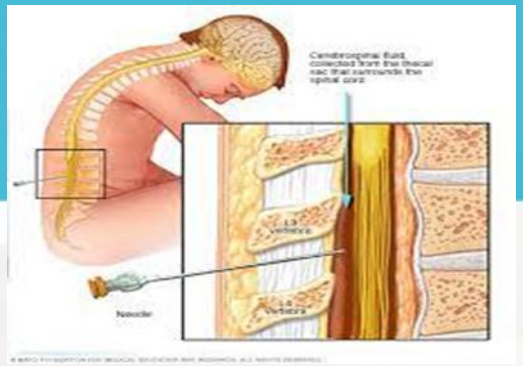
- More common in patients with AIDS, regardless of the presence or absence of CNS involvement.
- The disease includes the presence of hard erythematous nodules or skin ulcers.


Diagnosis
History& C.P.
Direct
Indirect

Clinical

History of wearing contact lenses+ clinical manifestations.

Direct



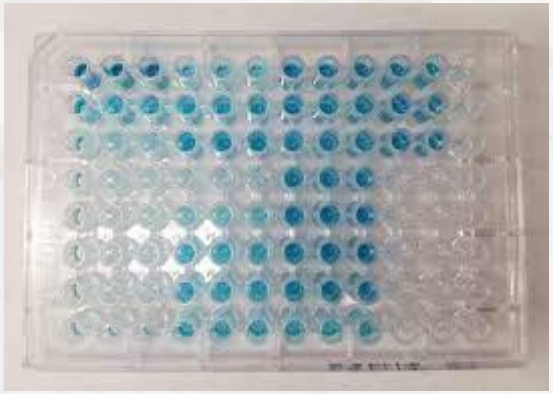
- Granulomatous Amebic Encephalitis (GAE) and disseminated infection are more difficult to diagnose and are often at advanced stages.
- Definitive diagnosis is made by examination of tissue and, rarely, by cerebrospinal fluid (CSF) analysis.

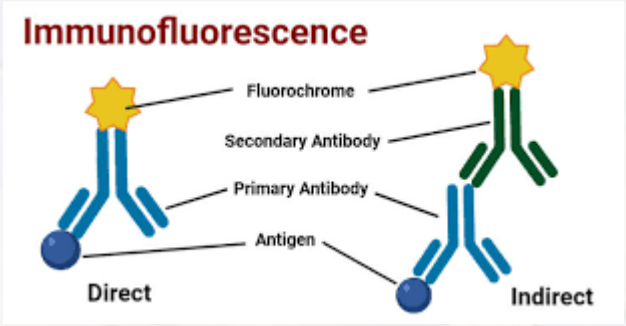
- CSF examination to exclude bacterial infection. No *Acanthamoeba* have been isolated from CSF.

- By culturing biopsy specimen on non nutrient agar plates seeded with *E. coli* to identify the cyst and/or trophozoite.

Indirect

- Serological examination either for sera or for culture products.





Treatment

Brain lesions:

- Surgical removal
- No drug has been proved useful for treatment of GAE.
- Sulfa drugs have been demonstrated efficacy in experimental animals.

Ocular lesions: Ocular lesion can be treated by enucleating the ulcer followed by corneal transplantation.

Prevention

- Proper care of contact lenses
- Do not use home made saline
- Avoid wearing lenses while swimming
- Avoid exposure to contaminated water

QUIZ

1- Habitat of *Naegleria fowleri is* ……

a. Brain
b. Intestine
c. Eye
d. RBCs

2- Granulomatous amoebic encephalitis is caused by:

a. ***Naegleria fowleri***

b. Acanthamoeba spp.

c. Entamoeba histolytica

d.Trypanospma spp.

Acute primary amoebic meningeoencephalitis is caused by:

a. ***Naegleria fowleri***

b. Acanthamoeba spp.

c. Entamoeba histolytica

d.Trypanospma spp.

- ***Mention mode of transmission of***

Acanthamoeba spp ?

- **What is the causative parasite and Clinical manifestations of Acute primary amoebic meningoencephalitis ?**

Reference

Henry's Clinical Diagnosis and Management by Laboratory Methods MEDICAL PARASITOLOGY

https://0810fk5ao-1104-y-https-www-clinicalkey-com.mplbci.ekb.eg/#!/browse/book/3-s2.0-C20180017521

Richard A. Mcpherson, Matthew R. Picnic (2021)
Henry's Clinical Diagnosis and Management by Laboratory Methods, Twenty Fourth Edition chapter 65 MEDICAL PARASITOLOGY Elsevier June 1, 2021

Recommended :

2-**Textbook_of_MEDICAL_PARASITOLOGY**
https://www.academia.edu/44759301/Textbook_of_MEDICAL_PARASITOLOGY_Textbook_of_MEDICAL_PARASITOLOGY

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CK Jayaram Paniker (2007): Textbook of MEDICAL PARASITOLOGY Textbook of MEDICAL PARASITOLOGY. Sixth Edition: 2007. ISBN 81-8061-937-0.

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